PublisherInfo		
PublisherName	:	BioMed Central
PublisherLocation	:	London
PublisherImprintName	:	BioMed Central

Epstein-Barr virus in breast cancers

ArticleInfo		
ArticleID	:	3629
ArticleDOI	:	10.1186/bcr-1999-66607
ArticleCitationID	:	66607
ArticleSequenceNumber	:	49
ArticleCategory	:	Paper Report
ArticleFirstPage	:	1
ArticleLastPage	:	4
ArticleHistory	:	RegistrationDate : 1999–8–25 OnlineDate : 1999–8–25
ArticleCopyright	:	Current Science Ltd1999
ArticleGrants	:	
ArticleContext	:	1305811

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Keywords

breast cancer, Epstein-Barr virus, metastasis, pathogenesis

Introduction

The Epstein-Barr Virus (EBV) is associated with the development of a range of different human cancers, including several types of carcinoma. A correlation between EBV-associated lymphomas and a high incidence of male breast cancer has been reported, and furthermore, EBV-associated lymphomas have been reported to be localized in the breast. Two studies have detected EBV in 20-40% of breast tumors investigated. These observations have led some investigators to suggest that the virus may play a role in the development of breast cancer.

Aims

To investigate the presence of EBV in human breast cancers.

Comments

EBV has long been implicated in the development of several human cancers, and previous work has found EBV to be present in a small proportion of malignant breast samples. This article describes evidence of the presence of EBV in a large subset of invasive breast carcinomas. The correlation of EBV with factors associated with poor outcome suggests a role for the virus in the pathogenesis of these more aggressive tumors. The point in tumor development at which EBV infection occurs remains to be determined, although the data presented here indicate that the tumor cells may have been infected before metastasis took place.

Methods

One hundred consecutive biopsy specimens of primary invasive breast carcinoma, as well as 30 normal tissues adjacent to breast tumors, were obtained without preselection. DNA was amplified by the polymerase chain reaction (PCR) with primers covering three different regions of the EBV genome. Southern blot analysis was performed using a labeled EBV restriction fragment as the probe. Infected cells were identified by immunohistochemical staining using monoclonal antibodies directed against the Epstein-Barr nuclear antigen 1 (EBNA-1).

Results

EBV was detected by PCR in 51% of the tumors studied, and in only 10% of the healthy tissue adjacent to the tumor ($P < 0.001$). The presence of the EBV genome in breast tumors was confirmed by Southern blot analysis, further suggesting the predominant source of EBV DNA is the tumor epithelial cells, and not lymphoplasmocytic infiltration. No association was observed between EBV detection and tumor histology or a range of other prognostic factors, including age at diagnosis, tumor size and menopausal status. The proportion of EBV-positive tumors was, however, statistically significantly higher in carcinomas of higher histologic grade. An association between EBV-positive tumors and steroid-receptor-negative tumors and nodal status was also statistically significant. Immunohistochemical staining of EBNA-1 confirmed that EBV expression was restricted to the tumor cells, and that a variable but appreciable number (5-30%) of those cells were infected by the virus.

Discussion

Of the primary breast tumors studied, 51% showed the presence of EBV, a proportion significantly higher than that in adjacent healthy tissue. For the first time, a statistically significant relationship was demonstrated between EBV-positive tumors and several poor prognostic factors, including steroid receptor negativity, high histologic grade and lymph node metastases. The association with axillary lymph node invasion suggests that infection with EBV may be related to the high metastatic potential of the tumor.

References

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